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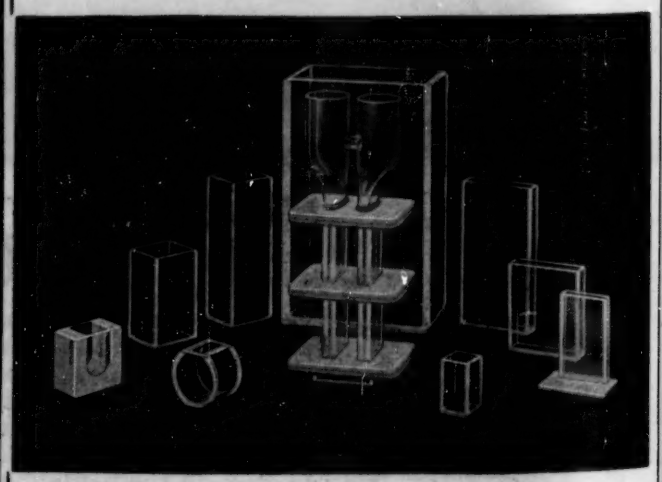

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RESEARCH AND THERAPEUTICS[1]

By Dr. AUSTIN E. SMITH

SECRETARY, COUNCIL ON PHARMACY AND CHEMISTRY, AMERICAN MEDICAL ASSOCIATION

DURING the year 1942 nearly one tenth of the entire population became a hospital bed patient. One person entered a hospital in the United States as a patient every two and a half seconds. Surgical operations were performed at a rate of one to each 5.6 seconds and the hospital birth rate exceeded three live babies to the minute.

This represents only a part of the total illness in this country and is, of course, only a fraction of the illness prevalent throughout the world. By the time the war is over such figures when compared to world-wide statistics will be infinitesimal. At the recent National Conference on Planning for War and Post-war Medical Services a number of papers were presented to show post-war medical needs. Obviously the papers could not be specific in details as exact estimates for post-war needs are impossible to determine at this time, but they did give an indication of the future enormous requirements from the drug manufacturers. Will the demands be met entirely by current drugs or will there be available a host of new agents? With American medicine encountering diseases alien to these shores through participation in world-wide health problems and the return of infected troops, new and more effective agents will have to be provided.

At present the drug-manufacturing industry is faced with many problems—two major ones are increasing reductions of certain basic materials and increasing demands for Lend-Lease, armed forces and civilian use. The probable needs in the early post-war period stagger the imagination. As each manufacturer will have to give careful thought to the optimal use of his supplies, there is afforded a good opportu-

[1] Read before the 1943 Annual Convention of the American Drug Manufacturers Association, Chicago, May 3, 1943.

nity to discard old, outmoded and comparatively useless agents. Here is an excuse to bite a hand that offers food with no disastrous results. If these deletions are offset by the introduction of new and truly effective agents there will be nothing lost but much gained. Undoubtedly successful survival and expanded competition after the war will depend largely on the establishment and output of research departments. Recently we were told of a basic list of drugs which will be needed in occupied countries as they are liberated, that the pooled resources of the world will be taxed to the utmost and that the medical profession and medical resources of this country will be called upon increasingly to meet the needs of the world for medical care and medical services. If our own physicians, scientists and educators are sent elsewhere in the world to administer to the ill and to organize health and educational programs, American drugs will be in demand not only because of availability but also because of familiarity.

Research Participation

The degree to which research is dependent on therapeutics and therapeutics on research is undeniably appreciated by the medical, dental and pharmaceutical professions and drug manufacturers. The needs for research and progressive therapeutics are evident. The physician and the drug manufacturer are responsible for the prevention, diagnosis and treatment of disease. Their course of action is equally evident. Circumspective thought must be given to the inadequacy of existing treatments, the development of new ideas, their laboratory and clinical trial, their practical application. If it is the duty of the physician to prevent illness, to supply proper medical care for those who are ill and to encourage medical investigation, is not the drug manufacturer faced with the same responsibility? If the health of a nation depends on medical attention, does it not also depend largely on those who supply part of the treatment? And if the medical profession on the firing line needs assistance, should it not be able to turn freely and expectantly to those in the advance supply line?

Often one is asked who should take the initiative in drug research, the physician or the manufacturer. The answer is simple: Every one capable of doing meritorious work should participate. No one will wait for his neighbor if there is sufficient interest in the project. This has been especially true in the last decade and will continue after the war. During normal times research provokes increased business and better health. During times of war it is a patriotic duty to increase research activity; new agents are needed; faster methods of manufacture are essential; better storage conditions are helpful. In the top-notch center such responsibility is shared by all participants as they are interested not only in progress in their respective fields but in survival of their own places in these fields.

There is more to research than developing a new extract or a synthetic compound. The new agent must be carefully studied in test-tubes, on bacteria or animals and in the human. Such studies are complete only when proper working facilities are provided. If the manufacturer has not the space, equipment or trained personnel, the work can be completed elsewhere. When there is joint research the drug house and the investigating physician have certain responsibilities to each other: these should be clear-cut and well understood before any action is begun; otherwise friction and discontent will develop.

Progress in therapeutics does not depend entirely on the development of startling new drugs. Contributions may be offered through studies on diets, atmosphere, clothing, habits; in fact anything which will aid in the prevention and treatment of illness and increasing life expectancy is worthwhile. Too often improperly trained or equipped groups spend prohibitive amounts of time and money searching for miracle agents which are beyond their scope and overlook something practical close at hand.

Changes in Therapeutics

There are many who fail to realize how much progress has been made in the last twenty years in materia medica. In a certain book published in 1899 may be found ingredients of compounds commonly used at that time. One "uterine tonic and restorative" contained unicorn root, catnip, cramp bark, mitchella, cohosh, cinnamon, orange peel, caraway, sugar, diluted alcohol and water. How much different was this formula from those used by civilizations many centuries older! While many such mixtures are still evident they are fairly rapidly disappearing, largely because of the demands of science and of the spirit of competition. In fact, how often to-day do we hear the term "uterine tonic and restorative." A "neuralgic pill" consisted of extract of hyoscyamus, extract of conium, extract of Ignatia bean, extract of opium, extract of aconite, extract of cannabis indica, extract of stramonium and extract of belladonna. A treatment for diarrhea and dysentery offered blackberry root, galls, cinnamon, cloves, mace, ginger, blackberry juice, simple syrup, glycerin and diluted alcohol. Remedies for "female disorders," asthma, baldness and "blood purifiers" contained no end of ingredients. Such mixtures were frequently used less than forty years ago, even though the treatment of disease is

almost as old as man. It takes no trained eye to scan scientific literature and perceive that therapeutics has progressed by leaps and bounds in the last twenty years. Such progress has been born directly of research. Were it not for research the world would still be lacking serums and vaccines, sedatives, anesthetics, vitamins, anti-infective agents and countless other agents. Were it not for research there would be no high-caliber medical, chemical and other meetings, nor would there be the galaxy of published papers now at our command.

Expediting Research

Unquestionably there are delays in research and therapeutic advances—one of the greatest contributing factors is probably misunderstanding: misunderstanding by the physician, educational or research center and manufacturing directors of what a drug manufacturer is capable of doing; misunderstanding of what may be expected of and by an investigating clinician, chemist or pharmacologist or other scientist; and misunderstanding of what may be expected of and by a research center. Such misunderstanding has long served to perpetuate existing confusion, and yet it is surprising to observe how few attempt to ascertain and remove the cause of the confusion.

The first step for any proposed investigation is a consideration of the practicality of the problem and an outline of the program. Then must be determined the limitations of the investigator or the manufacturer. Frequently there is failure to realize existing potentialities and to make the most of these. Of equal frequency is failure to realize one's limitations and the end conclusion is a dismal lack of success or, at the most, uncritical results. Perhaps part of the fault lies in the assigning of incompetent individuals or groups to make the necessary surveys; such incompetence may exist any place along the line of proposed action. Unless the causes for confusion and misunderstanding are removed no individual or organization can hope to contribute the best to the maintenance or promotion of health.

Having decided what can be done, the next decision concerns how it can be done best. Frequently this raises the question of expansion. Expansion, whether it be by a drug manufacturer or by a center of investigation, must be made on a solid foundation. Sometimes expansion is impossible, in which case it is much better economically and otherwise to remain firm and avoid the risk of regression. Too often there is failure to realize that the promoter and investigator are best suited for a particular type of job which could make them outstanding in the one field but which would leave them far behind if they attempted to work in totally alien fields. It is through a proper evaluation of one's scope of activity that we expect to be able to shrug aside such headlines as the following that appeared in a recent trade journal, "German Economic War Purposes Holds World Chemical Control." In view of what has been observed of American drug ingenuity, how can any other nation hold chemical control unless that nation is deliberately permitted to do so? Cheerfully on the same day there appeared an article entitled "Anti-Malarial Ammunition. Synthetic Drugs Will Match Former Quinine Production in Curative Power." When one can speak of the manufacture of billions of tablets of atabrine, tons of vitamins and hundreds of tons of sulfonamides, things which have been developed within a few years, one realizes the tremendous possibilities of research and therapeutics. One has only to look at the statistics provided in bulletins offered by the Department of Commerce and the U. S. Tariff Commission to comprehend the diversity and enormousness of drug manufacture in the United States.

Cooperation

Perhaps the thing which is contributing most to the present stage of development is the close cooperation of various sciences and specialists. Engaged on common problems may be found biochemists, organic chemists, physiologic chemists, pharmacologists, immunologists, clinicians, pharmacists, dentists, etc. Truly no one individual nor any one science stands alone as they may have in the years gone by. Contributions to materia medica have been made by practically all sciences; in no other field is there any closer affiliation between varied interests. In no other field can racial and national differences be more completely forgotten. Undesirable secrecy is disappearing, distrust is showing hopeful signs of receding and ideas are exchanged freely in conferences and at scientific meetings. Daily there are appearing announcements of new drugs, new research, new sources of outlet and agreements with other nations to promote hemispheric trade. Cooperation with adequate evaluation of one's scope plus a fair amount of aggressiveness will provide more drugs, better therapeutic technics and opportunities to partake in the existing agreements and others which will follow. Willingness to cooperate on medical problems not necessarily restricted to this country can be a most forceful weapon in promoting international developments, understanding and good will.

Summary

Progressive therapeutics depends on research, but at the same time it is a marked stimulant for promoting research. Through research will come much of the

post-war advancement which may occur in medicine and allied sciences, drug manufacturing and educational centers. Success and survival will depend not only on cooperation, leadership and a shrewd business sense but on an adequate appreciation of opportunities, limitations and the value of fostering research by providing grants and fellowships. Much material assistance can be provided with mutual gain for all participants when such fellowships are established. This gain may extend past current problems into lifelong associations. If the manufacturer recognizes his opportunities and obligations and forges ahead to challenge or accept them instead of remaining on the defensive, there will be less likelihood of being fettered by purblind policies. Each one interested in research and therapeutics has responsibilities peculiar to himself, but there are few, regardless of occupation, who, at the completion of a job well done, does not feel as Pasteur, who said of the researcher:

> It is indeed a hard task when you believe you have found an important scientific fact and are feverishly anxious to publish it, to constrain yourself for days, weeks, years sometimes, to fight with yourself, to try to ruin your own experiments and only to proclaim your discovery after having exhausted all contrary hypotheses.
>
> But when, after so many efforts, you have at last arrived at certainty, your joy is one of the greatest which can be felt by a human soul, and the thought that you will have contributed to the honor of your country renders that joy still deeper.

THE INTRODUCTION OF NEW VIEWPOINTS AND SCIENTIFIC CONCEPTS IN GENERAL BOTANY[1]

By Dr. J. FISHER STANFIELD

CHICAGO TEACHERS COLLEGE

IN any consideration of the approach to be utilized in presenting general botany to students of random selection and average ability, it is obviously necessary to examine with care the general aims of such an offering. It is also necessary, in this transitional period in methodology, to examine critically all current tendencies and evaluate them; one must further correlate the last named with certain recognized, sound and acceptable principles of scientific instruction at the college level. Lastly, it is imperative that we interpret and apply all controversial procedures within the limitations of personnel and equipment of the average undergraduate college.

Work at the college level is not to be confused with that of elementary grades in which the teacher is concerned with immature, plastic minds. Neither is it to be considered as similar to that offered at the secondary-school level, in which we have no selection of students whatsoever other than natural and no aim other than very generally cultural. College botany is a course offered to at least a pseudo-mature student body in which some degree of selection has operated, since only a very small percentage of high-school graduates enter college. At the worst, we are thus facing a selected group of students who should begin to divorce themselves from an immature approach to their studies. The fact that only one per cent. of the students taking general botany continue in the subject for advanced work does not change the last statement to any degree. One cogent, major aim of teaching remains fundamentally the same: a flexible and inspirationally directed assimilation of factual data and principles of proven worth with applications to those life situations within the mental scope and experience of the individual in question; factual data with which to achieve a concurrently developed, intelligent, appreciation with a concomitant curiosity as to plants, their reactions to factors in their environment, and their economic or biotic aspects, *i.e.*, plant sociology.

With these fundamentals, the fad of the moment, the latest tendency (often revived) of the professional pendulum swinger in methods, is simply incorporated into the inescapable and irreducible fundamentals of any science—namely, the assimilation of sufficient data upon which to laminate intelligent concepts; the precursors of a lasting constructive curiosity fostered by satisfaction in mature achievement rather than the immature, rambling questioning of untutored minds. Thus, whether you are striving to develop a sense of citizenship, achieve indefinite sociological aims, or direct a student in the first steps along the road to a professional scientific career, it is here in this freshman course that we must somehow bring him to see the necessity of accumulating data, developing powers of observation, achieving mental discipline, correlating factual agenda with immediate and general environment, and, finally, bring about the development of an inherent appreciation and curiosity

[1] A paper presented at the Symposium on the Teaching of Botany at Dallas in 1941 before the Botanical Society of America and the American Society of Plant Physiologists.

relative to the plant world—an inspiration for further work—a sense of the challenging problems within the field of botany and its varied fields of specialization.

College botany is in a state of flux and may it never become static. Students are adjusting themselves to a rapidly changing world; curricula are changing; progress demands a treatment of recent scientific advances as well as the more stereotyped textbook essentials—applications of new concepts to the fundamental agenda so well known to us all. It is with some of these concepts that we shall now proceed.

There is a wide gap between formal research—pure science—and the mental set of the average freshman. It is possible, however, to adapt modern concepts to the course of study and thereby bring to the student not only a greater appreciation of plant science and its ramifications but also the awakening of curiosity and the awareness of plants as entities—as complex organisms in a living world.

We can then consider the plant as a whole, as an entity, and interpret morphology, physiology, etc., as intergrading biotic, dynamic living forces. This work may be simplified greatly if the student himself actually grows and tends plants over a period of time. The Chicago Teachers College is fortunate in having available greenhouse facilities so that each student actually has the experience of tending seven square feet of soil from the preparation of the seed bed in the benches to the harvesting of fruit and seeds. Seeding, transplanting, potting, rooting of cuttings, soils and fertilizers, and factors of growth may be considered in one situation and the writer has yet to see the student who does not feel a just glow of pride in his achievements. In this particular institution this practical, horticultural experience is a part of the required course of study for every freshman and is thus carried into their ultimate professional activities.

It is thus possible for the student to observe, with proper suggestions, that the life cycle of a typical flowering plant is really a series of phases. From the germination of the seed the vegetative phase is observed with growth and accompanying activities. Buds arise and flowering proceeds with the stoppage of growth common to this phase as shown clearly in recent work with tomatoes. Then follows the production of the fruit with a quickened pulse, so to speak, and ultimately the senescence of this individual plant or its parts. Even though a student may not realize or grasp fully all the details in the limited time available, the seed of an idea is fixed; namely, the plant as a whole with integrating, though definite, phases of development. With even a low ebb of interest, the most negative student may note his mistakes in tending the plants, observe variations in the growth of different species, see aberrations in certain phases of growth due to critical factors, become sensitized to factors in general and thus conceive of plants as living, changing complexes passing through definite phases in their development and reacting accordingly. It isn't difficult for a student to understand germination, embryos and the origin of tissues when he sees them unfold before his eyes. He may even think of a plant as a result of its past rather than its present in having presented to him facts relative to induced phenomena at certain stages in its embryology; for example, light and temperature effects in photoperiodism and vernalization. One may gradually perceive that the study of growth is a study of the differences developing from similar cells arising in meristems and growing into various structures. Physiological changes in these cells can then be considered in terms of environment and heredity. The firing and stimulation of the imagination and the correlation of varied factual data in the mind of the student are of the greatest value in these considerations.

Germination of seeds in glass containers may be used as illustrative material for many of these phenomena; at least a cotyledon and plumule become realities. In lieu of greenhouse experience, if space is available, even a potted plant or an experiment in hydroponics is feasible. The latter is particularly appropriate in the light of common usage both commercially and in the home. An understanding of the simple requirements for fertilizers can be included, although more practical knowledge is gained from a study of soils. In any event, the actual growing of plants is a vital requisite for successful work in general botany and certainly for the introduction of much colorful and challenging data.

In connection with the morphology of seedlings and growth a student can comprehend the sensitive loci of stimulus and response in plants by the use of simple experiments. Simply placing a box over a plant or stringing a few light bulbs brings a vivid appreciation of the phenomena of photoperiodism, and the seasonal blooming of common garden plants becomes significant to the student. Shading a part of a plant definitely connotes transport of a hormonal stimulus or inhibition in plants. Seasonal variations are clarified and gardens become something more than simply aggregations of miscellaneous plants. The student again thinks of a plant as an individual with loci of responses and transport of chemical determiners; thus, subsequently, some form of concept relative to meristems, primordia and manner of growth gradually evolves. With mitosis as a

requisite, the use of colchicine is introduced and, if successfully applied, evolution occurs in the morphological change of the tissues reacting and the vista of future economic possibilities spreads before them. Further types of induced mutations are but another step in the line of thought, and variations in turn are assimilated with enlarged understanding of progressive development; at least to a greater degree than before.

The concept of control of plant development by internal forces is one of fundamental significance. Hormones have become a by-word of the layman and vitamins are a part of the average vocabulary. Auxin, as a collective term, is used quite freely and will soon become a part of all courses. While it is not practicable to utilize auxin as such, there is no dearth as yet of synthetics. With the varied phenomena attributed to these complicated chemical factors—growth promotions, growth inhibition, differentiation of tissues, flowering, fruit development—the concept of hormonal control assumes significant proportions as a causative factor. The interrelations of plant parts may be stressed in this connection; this is a further approach to the concept of plants as entities.

Bud dominance is easily introduced in varied ways. Apical dominance in potatoes, for example, and its importance in planting can be stressed and in some instances chemicals may be used to break such dominance. Apical dominance and inhibition of later growth as illustrated in tree form are easily seen and the simple procedure of pinching back a plant grown in the greenhouse with the subsequent development of buds indicates a change in the hormonal balance; for example, a reversal of the floral to the vegetative phase with its concomitant growth as compared with the more static phase of flowering.

The rooting of cuttings with the appearance of adventitious roots brings the attention once again to hormones and vitamins. It is of never-failing interest to the student to observe the formation of roots on various plant parts by means of the rooting hormones. Synthetic hormones in lanolin paste brings roots from stems and with proper application brings prototropism into clear focus as shown by the bending of stems when hormones are applied. The action of hormones in geotropism then becomes more clear. To see roots growing and covering stems by adding a few milligrams of an acid to the soil is also striking. Once the concept of hormones is established, parthenocarpy may be introduced with varied materials in keeping with the latest findings. From this approach, pollination and fertilization assume realistic proportions since basic understanding is present. A seedless tomato—a swollen ovulary—and then economic applications and the experimental work on premature fall of fruits and the delay of opening of blossoms to avoid killing frosts. The plant sciences begin to assume significant aspects in the eyes of the student—a necessary and vital prerequisite for positive and challenging interest with a fixation of facts rich in either professional or cultural connotations.

In addition to these modern approaches, the subject of vernalization and dormancy is always of interest; all students respond to the unusual, and certainly the explanation of these reactions can not fail to fall into this category. In addition, it is not at all difficult to stress the economic aspects of such work; either the latter or its application and relationship to man as the perpendicular pronoun will achieve the same result. Common bulbs may be treated and certain aspects of dormancy in general may be clarified. Dormant twigs are always potent illustrative material with morphological applications. Many misconceptions born of extravagant claims relative to vitamins and hormones may be corrected in such studies.

In general, these engrossing applications, in addition to experience in the actual growing of plants as practiced in the greenhouse, have caused the plant as a whole to assume a colorful significance in the life of even a casually interested individual. An integration has occurred; roots, stems, leaves, flowers, fruits, seeds—the student has run the gamut of them all—has observed the plant in all its phases of growth from the first cotyledons to the achievement of its ultimate goal—the seed. Perhaps even a casual understanding of vernalization and respiration has brought to him a sense of the living qualities—the reactions of dormant embryos or partly stimulated embryos to factors in the environment. Primordia are not simply morphological units or divisions; they are regions from which develop the resultants of heredity and environment, shaped by factors controlled by hormo-vitamin combinations, possessed of a phasal ontogeny and in a constant stage of change —an individual living through the infinitesimally short interphase of an evolutionary sequence.

Perhaps none of us can achieve all these correlations; not all instructors, for example, can provide actual, continuous, hands-in-the-dirt experiences. This brief presentation is by no means complete; the instructor may add others in respective fields of specialization and adapt them to presentation of material. All of us can, however, amplify our fundamentals with modern approaches and concepts—glorify our essentials with inspirational explanation of observed phenomena and thus achieve in a mature fashion, in a manner in keeping with the intelligence of our students at the college level, those aims so briefly entertained in the opening paragraph.

OBITUARY

LESLIE TILLOTSON WEBSTER
1894–1943

LESLIE TILLOTSON WEBSTER was born in New York City on July 23, 1894. After graduating from Amherst College in 1915 he studied medicine at Johns Hopkins University, where he graduated in 1919. After one year in the department of pathology at Johns Hopkins Medical School, he joined the staff of The Rockefeller Institute for Medical Research in 1920; he remained at the institute, of which he became a member in 1934, until his death on July 12, 1943.

From the beginning of his scientific career, Dr. Webster was strongly attracted to the study of factors operating in the spread of infectious diseases in different kinds of populations. When he began his work it was a matter of common observation that epidemics arise in the midst of a population, reach a maximum and then, after killing a number of individuals, wane. The reason for this cyclic course was attributed to chance contact with an infective agent. It was assumed that a highly virulent strain of an infective agent overcame the resistance of equally susceptible individuals of a population, thereby starting an epidemic. Then, as the number of cases increased, the elimination by death of many individuals in the population took place accompanied at the same time by active immunization of those that had suffered a sublethal infection. It was assumed that such a process eventually brought to an end an epidemic, leaving behind only individuals with an increased resistance. In this conception of epidemics little attention was paid to the host factor. Dr. Webster's work proved that in a given population individuals differ greatly in their susceptibility to infection, and that the host factor plays an important role in the rise and fall of epidemics.

By careful and painstaking work Dr. Webster proved that individuals have different degrees of resistance and susceptibility to infection, that these qualities are segregable and inheritable and that strains of animals can be developed by proper inbreeding so that some are highly resistant while others are exceedingly susceptible. By using properly bred animals he proved that in an experimental epidemic there is no need for an infective agent of exceedingly high virulence in order to start an epidemic; it is sufficient that the number of susceptible animals constitute a certain proportion of the population. The epidemic continues as long as enough susceptible animals are present, and, when the number of susceptibles reaches a certain low level, the infective agent through lack of proper soil ceases to be active, thus ending an epidemic. The individuals surviving an epidemic are resistant, not through a process of active immunization but through their inherited qualities. This was Dr. Webster's fundamental contribution to epidemiology and one that has had a marked influence on all modern work on infectious diseases.

In the field of virus infections, Dr. Webster's contributions have been many and important, especially his studies on rabies. Through his investigations more accurate methods of diagnosis were developed and his studies on antirabic vaccines led to a better evaluation of their potency and to the use of ultraviolet light in their preparation. His studies of human encephalitides has thrown light on many problems in this field; he particularly showed the value of albino mice in investigations of these maladies.

At the time of his death Dr. Webster was fully occupied by the study of the influence of dietary factors on resistance and susceptibility to infectious diseases. It is most unfortunate that his death deprived him of the pleasure of harvesting the fruit of this work. To his friends and to those who had the great privilege of being associated with him in scientific endeavor, his death has caused an irreparable loss; his critical scientific qualities, his kindness and devotion to his friends will long be remembered.

J. CASALS
T. M. RIVERS

WALTER E. McCOURT

PRIVATE funeral services were held on June 1 for Walter Edward McCourt, assistant chancellor of the Washington University, St. Louis, who died suddenly of a heart ailment on May 30 at his home.

Dean McCourt, fifty-nine years old, had been a member of the faculty since 1906. He had been in charge of the department of geology and geography since 1907 and served as dean of the Schools of Engineering and Architecture from 1920 to 1928.

Besides being one of the most popular teachers at the university Dean McCourt was active in scientific and discussion groups, both of a local and national nature. He was a former president of the Engineers Club of St. Louis, and for twenty-five years served as secretary of the American Institute of Mining and Metallurgical Engineers for this district.

Born in Brooklyn, N. Y., he received an A.B. degree in 1904 and an M.A. in 1905, both from Cornell University. He joined the Washington University faculty the following year. He was first an instructor in geology; was promoted to assistant professor in 1907, to associate professor in 1912 and three years later to full professorship.

He was a celebrated authority and lecturer on vol-

canoes, national parks and mountains. His classes at the university were among the favorite science courses. During his travels he had collected a valuable collection of picture slides which he often used with his lectures.

LEWIS F. THOMAS

WASHINGTON UNIVERSITY,
ST. LOUIS

DEATHS AND MEMORIALS

DR. IVIN SICKELS, professor emeritus of geology at the College of the City of New York, died in his ninetieth year on August 5.

THE death is announced of Baron Gerard de Geer, from 1877 to 1924 professor of geology at the University of Stockholm, founder of the Geochronological Institute there and an authority on glacial and post-glacial problems. He was eighty-four years old.

THE *Journal* of the American Medical Association reports that a public campaign to raise at least $300,000 to be donated to the University of Cincinnati College of Medicine as a fund dedicated to the memory of Dr. Mont R. Reid was opened on July 12. The fund is to be used to supplement the regular budget of the College of Medicine and is intended "to honor the memory of a great citizen, to advance the cause of medical science and teaching and to promote the health of our community." An annual deficit varying from $18,000 to $25,000 has been met usually through the personal efforts of Dr. Reid.

SCIENTIFIC EVENTS

THE ROSS INSTITUTE OF TROPICAL HYGIENE

IT is pointed out in *The British Medical Journal* that the part played by the Tropics in providing indispensable products of all kinds has never perhaps before been so forcibly brought to the notice of the public as now. Nor in this connection has the importance of malaria and the need for controlling this most deadly of tropical diseases been so clearly demonstrated. Measures of control of malaria have now been developed in many parts of the world, but in none has progress in this respect been more conspicuous than in India. Particularly has the work of the Ross Institute of Tropical Hygiene (India Branch) in the Indian tea, jute and mining industries been a striking example of such progress. We have previously drawn attention to the part played by the institute in coordinating the resources of individual interests in these industries and in organizing and developing systematic research and active prosecution of measures throughout the many gardens, estates and labor forces concerned. The *Journal* summarizes as follows the information given in the annual report for 1941–42:

Among contributors to the cooperative action initiated by the institute are listed over twenty agents and companies controlling more than 200 estates, with a total acreage of nearly half a million; extracts from reports by medical officers and others give evidence of the scale and beneficial results of the measures undertaken. In the account of the year's activities malaria control naturally takes first place, and some interesting facts are given of the result of anti-malaria work on a number of estates. Methods of biological control have been widely made use of, because owing to their cheapness and permanent character such measures have largely eliminated the high recurrent cost of oiling schemes. There are now at least 4,000 miles of streams and drains on tea estates in which the breeding of *Anopheles minimus*, the chief malaria carrier in this region, has been controlled by the "dense shade" method, whilst the regular training and cleaning of streams and the institution of "flushing" devices and other anti-larval operations have been widely extended.

Perhaps the most immediately interesting part of the report concerns the branch's activities in relation to the military situation in India. The invasion of Burma by the Japanese has introduced many acute problems, not the least of these being malaria in the frontier districts and among refugees passing into India by this route from Burma. Dr. Ramsay, principal of the India Branch, has with his great knowledge of the local malaria problems involved been able to give much help, at their request, to the military authorities. The branch has also been able to forward the war effort by providing trained Indian malaria surveyors. About 600 Indians, many of whom have volunteered for service, have now been trained at Ross Institute training centers. Several British medical officers formerly employed by the tea industry are also now, as a result of training and experience in anti-malaria work, rendering invaluable service as malariologists with the Army in different theaters of the war. The report notes the retirement for health reasons of Dr. David Manson, in whose laboratory at Cinnemara much research work has been carried out and over 200 malaria surveyors trained. Mention is also made of the very valuable results from the researches of Dr. Muirhead Thomson, of the London School of Hygiene and Tropical Medicine, upon the bionomics of the carrier species *A. minimus*, whose life history has been intensively investigated in the field.

THE BUDGET OF THE UNIVERSITY OF WISCONSIN

THE budget of the University of Wisconsin for the 1943–44 fiscal year, including funds for teaching and

training on a twelve-months basis, was adopted by the Board of Regents at its last meeting.

The budget for the fiscal year, which began on July 1, amounts to $7,205,160 for all educational and general expenditures and for all extension and public service work.

The figure represents an increase of $453,284 over the budget for 1942–43—an increase made necessary largely because of the fact that the university is now operating on a basis of three semesters instead of two semesters each year.

Education and general expenditures for 1943–44 will amount to $5,573,928, while extension and public service funds amount to $1,631,232. Some of these funds come from the state, others are earned in the form of fees, etc., while the remainder is paid by the Federal Government for the training of armed forces.

The budget makes provision for the year-round teaching load for both civilian and military students. The estimated enrolment includes approximately 1,900 civilian students in the full summer semester, 1,500 in the six and eight weeks' summer session, 5,000 civilian students in the regular academic year beginning in September, and 1,500 military students.

Included in the later group are the army air forces meteorologists, navy engineers, army basic phase, army foreign area and language and both army and navy medical students. In addition to these military students, who will be pursuing regular courses of instruction, the university will continue to train about 2,000 navy radio operators, WAVES, SPARS and marine women, navy cooks and bakers, and navy pilot trainees for whom instruction is separately financed.

It is estimated, therefore, that the enrolment during 1943–44 will consist of approximately 5,000 civilian students and nearly 4,000 military students or a grand total of 9,000 students.

AFFILIATED HOSPITAL UNITS FOR CIVILIAN DEFENSE

IN the *Journal* of the American Medical Association for June 26, attention was called to the fact that two hundred and fifty-one hospitals and medical schools have been invited by the Surgeon General of the U. S. Public Health Service to organize affiliated hospital units of the Emergency Medical Service of the U. S. Office of Civilian Defense. Already more than a thousand physicians and dentists have applied for association with these units.

Members of the staffs of affiliated units are commissioned in the inactive reserve of the U. S. Public Health Service, generally with ranks equivalent to those of captain, major or lieutenant colonel in the Army. They remain on inactive status except when there is an emergency arising from an air raid or other grave wartime disaster. When called to active duty they then receive the pay and allowances of officers of equivalent grade in the armed forces. They are expected to furnish service only in their own or neighboring states, and their obligation ceases at the termination of the present national emergency. The nature of the service is recognized by authorization to wear a lapel button which indicates that they have enlisted for emergency service. They do not wear a uniform until called to active duty and need not purchase one unless directed to do so when called to active duty.

The Board of Trustees of the American Medical Association and the Directing Board of the Procurement and Assignment Service have authorized essential physicians to accept positions with these affiliated units. Some physicians have expressed the fear that acceptance of these commissions might involve them in a responsibility to the U. S. Public Health Service and might in some way encourage the acceptance by the profession of the proposed Wagner-Murray-Dingell bill. This is a misunderstanding. Those who become associated with affiliated units are under no obligation to serve in any other capacity, no matter what functions Congress may some day see fit to thrust on the U. S. Public Health Service. Duties of members of affiliated units are limited strictly to those which they have agreed to assume as a result of enemy action.

THE ASSOCIATION OF UNIVERSITY PROFESSORS OF THE ALLIED COUNTRIES

THE Association of University Professors and Lecturers of the Allied Countries in Great Britain, according to *The Times*, London, began at New College, Oxford, on July 17 the largest conference which it has held so far. The subject of discussion was the reconstruction of universities in the occupied and conquered countries of Europe after the war.

The conference, which was welcomed to Oxford by its president, Professor S. A. Glaser, Polish Minister to Belgium and Luxembourg, was given the Oxford background to its aims by the regius professor of modern history, Dr. S. M. Powicke. It will work in three main groups and many sections. The group dealing with arts will be under Professor J. A. Veraart, Netherlands; the group for science will be under Professor A. Photiades, Greece, and that on general subjects under Dr. Jean Timmermans, professor of physical chemistry at the University of Brussels and director of the Bureau of the International Union of Chemistry.

Among the subjects discussed were law, science and technology, economics, the modern humanities, history, medicine other than general science, and information for students. The meeting considered reports from the various sections which had been at work on the

possibilities of setting up an educational clearing-house for Europe and the need for establishing an international body for information and coordination concerning inventions and discoveries.

Professor Timmermans, who is Minister of Public Instruction in the Belgian Government and who has been a vice-president of the association, was elected president.

THE BRITISH STANDARDS INSTITUTION

AT the annual general meeting of the British Standards Institution, which was held on July 20, according to the account in *The Times*, London, Sir Percy Ashley, the chairman, reviewed the present position of the institution and the work of the past year. In the course of his address he said that the 8,000 or so members of the committees of the institution who gave their time voluntarily, often traveling far without reimbursement of expenses, would feel gratified that the Government had recognized the institution as the sole organization for the issue of standards having a national application and that it had decided to increase substantially the grant-in-aid which, during the coming year, would be approximately £12,500 or nearly double the former grant.

He stated that there were in current use about 1,500 British standards, and during the year under review 230 new and revised standards or amendments had been issued. Complete sets of British standards were available for inspection at British diplomatic and trade commissioner offices in 16 centers in the British Commonwealth, two in the United States, six in South America, six in Europe, one in Egypt and one in Persia. The collaboration with standardizing bodies, overseas, in so far as conditions now permit, continues to develop steadily. Copies of overseas standards are available in the library of the institution.

Sir Percy pointed out that the institution could look back upon a year of continued progress and increased usefulness. He said:

> I believe that those industries which have been long and closely associated with the development of the institution recognize fully the advantage of having a single, independent, national standards organization. But those others which are only now beginning to consider the opportuneness of the time for a standardization program covering types and sizes, trade terms, definitions and performance standards, may feel that the preparation and promulgation of standards is a matter of purely domestic concern, and should therefore be carried out solely by their individual trade associations.
>
> There has also been some tendency for Government departments to do standardization work in their own ways and on their own lines. I believe that both those courses are wrong in principle, and that the best results for any industry, and certainly for the industry of the nation as a whole, will be obtained only if all this work is carried on within a national organization such as the British Standards Institution, which can coordinate and guide all such action to a common end.

During the past year the income and expenditure had increased by about 20 per cent., and amounted to some £53,000. The sales of British standards had gone up 57 per cent. The number of contributing members had increased by 15 per cent.

A RESEARCH COMMITTEE ON CLIMATOLOGY

A RESEARCH committee on climatology has recently been established in the Section of Meteorology of the American Geophysical Union by C. W. Thornthwaite, the president of the section. It is intended to be a working committee whose main aim is the fostering of active research in climatology and the exchange of ideas among climatologists. It considers its sphere of interest to lie mainly in (1) physical climatology, (2) microclimatology, (3) statistical climatology, (4) applied climatology and (5) climatological instruments. The committee will encourage climatological research of high quality in order to increase the existing body of knowledge in climatology and will endeavor to cooperate with workers in neighboring fields who are confronted with problems of climatological interpretation. Among these fields of application of climatic research are geography, synoptic meteorology, agriculture and biology, medicine and public health and various phases of engineering.

The scope of the committee, therefore, is conceived on a very broad basis, and while the actual work will shift in emphasis from time to time from one to another of these fields, it is not the intention of the committee to limit the activities of its members at any time. The membership of the committee is to be expanded gradually as the work develops. The committee now consists of the following members: Phil E. Church, Alfonso Contreras Arias, Woodrow C. Jacobs, Helmut E. Landsberg, *chairman*, John B. Leighly, Albert E. Parr, F. W. Reichelderfer, A. K. Showalter, Robert G. Stone, C. W. Thornthwaite and H. G. Wilm.

It is hoped that the committee may serve as a clearing-house for information on research in climatology actually in progress. One of its first objectives is, therefore, to find out what research is now under way. The committee hopes to obtain the names of persons and institutions now engaged in such research, and information on the character of the active projects. The committee intends to foster an active interchange of ideas through establishment of connections with these research workers. Machinery is being set up to prepare bibliographies on various phases of climatology. As the need arises subcommittees will be formed to deal with various special fields.

H. D. HARRADON,
Secretary, Section of Meteorology,
American Geophysical Union

SCIENTIFIC NOTES AND NEWS

DR. PERRIN H. LONG, professor of preventive medicine at the School of Medicine of the Johns Hopkins University, is now a lieutenant colonel serving as medical director in the North African war theater.

DR. DONALD C. BALFOUR, director of the Mayo Foundation, has been elected an honorary fellow of the Royal Society of Medicine, London.

DR. ALEXEY NIKOLAEVICH BACH, biochemist of the University of Kiev, and Dr. Te-Pan'g Hou, Chinese industrial chemist, will be awarded honorary membership in the Society of Chemical Industry at a dinner meeting of the society to be held at the Waldorf-Astoria on October 22.

THE Clarke Memorial Medal for 1942 of the Royal Society of New South Wales has been awarded to Dr. W. L. Waterhouse, of the University of Sydney, "in recognition of outstanding contributions in the sphere of natural science, particularly in plant pathology."

AT a recent meeting of the Academy of Medicine of Cleveland, Dr. Howard Dittrick, for many years a member or chairman of the publications committee, was presented with the distinguished service award of the academy for 1943. The award consisted of a silver plate and went to Dr. Dittrick in recognition of his service to the academy over a long period of time.

THE doctorate of laws of the University of Leeds will be conferred on Professor H. S. Raper, Brackenbury professor of physiology at the University of Manchester, and the doctorate of science on E. V. Evans, chairman of the British Gas Research Board.

A DINNER in honor of Dr. Esther Rosencrantz, associate professor of medicine and lecturer in medical history and bibliography at the Medical Center in San Francisco, was given by fifty of her colleagues at the Palace Hotel on July 9 on the occasion of her retirement from the Medical School of the University of California after a service of thirty years. From 1920 to 1937, Dr. Rosencrantz was chief of the Tuberculosis Service at the San Francisco City and County Hospital.

THE American Society of Naturalists has elected the following officers to serve for the year 1943: H. J. Muller, Amherst College, *President;* B. M. [illegible]uggar, University of Wisconsin, *Vice-president;* A. C. Kinsey, Indiana University, *Secretary;* and M. R. Irwin, University of Wisconsin, *Treasurer.* The following were elected members of the society: Ernest C. Abbe, LeRoy Abrams, F. A. Beach, J. P. Bennett, James Bonner, Ralph Buchsbaum, Earl O. Butcher, Fred K. Butters, Wanda K. Farr, David R. Goddard, Karl C. Hamner, Edwin R. Helwig, Hope Hibbard, Theodore L. Jahn, John S. Karling, Stewart A. Koser, Alfred M. Lucas, Gordon Marsh, H. M. Parshley, Frederick V. Rand, P. L. Risley, Ralph Singleton, J. M. Webber and S. H. Yarnell.

THE interim Commission on Food and Agriculture, which was established by the United Nations conference at Hot Springs, Va., has elected as its permanent chairman L. B. Pearson, minister-counsellor of the Canadian Legation, and as vice-chairmen M. Pavel Tchegula, of the Soviet Purchasing Commission, and Tsou Ping-wan, of the Chinese Food Ministry.

COLONEL SIR A. STANLEY ANGWIN has been elected president of the British Institution of Electrical Engineers; T. G. N. Haldane and Dr. E. B. Moullin have been elected vice-presidents; and E. S. Byng has been elected honorary treasurer.

DR. EARL O. BUTCHER, professor of biology at Hamilton College, a member of the faculty for fifteen years, has resigned to join the department of anatomy of the New York University College of Medicine and Dentistry.

DR. HENRY N. HARKINS, of the Henry Ford Hospital, Detroit, has become associate professor of surgery at the School of Medicine of the Johns Hopkins University.

DR. ERIC OGDEN, associate professor of physiology at the University of California at Berkeley, has been appointed professor of physiology at the School of Medicine of the University of Texas, Galveston, and clinical physiologist to the John Sealy Hospital. He has been associated with the division of physiology of the University of California since 1929.

DR. STEWART C. THOMSON, assistant professor of anatomy at the Loyola University School of Medicine, Chicago, Ill., has been appointed assistant dean of the school. He succeeds Dr. John G. Powers, who will enter private practice. Dr. Francis J. Braceland, dean of the Medical School, is now in the Navy. Dr. Amedeo S. Marrazzi, assistant professor of pharmacology at the New York University College of Medicine, has been appointed professor and head of the new department of pharmacology.

ETHELWYN B. WILCOX has been appointed assistant professor of nutrition at the Utah State Agricultural College at Logan.

DR. O. N. ALLEN, professor of bacteriology and a former chairman of the department of botany of the University of Hawaii, has recently been named chairman of the newly established department of bacteriology.

THE U. S. Public Health Service has made a grant to Washington University to finance a cooperative study by Drs. M. Trotter and V. Lanier, of the department of anatomy, and Dr. Howard McKnight, of the department of obstetrics and gynecology, of the spinal dura mater and of the posterior surface of the sacrum in connection with the new method of continuous caudal anesthesia in childbirth.

DR. CHARLES S. HANES, chairman of the British Advisory Committee on Dehydration of the Combined Food Board, has been appointed director of food investigation in the Department of Scientific and Industrial Research.

DR. A. J. AMOR has been appointed chief medical officer of the British Ministry of Supply in succession to Air Vice-Marshal Sir David Munro, who has resigned to become medical adviser to the Ministry.

The Times, London, reports that Dr. C. M. Wenyon, F.R.S., will retire shortly under the age limit from the position of director-in-chief of the Wellcome Research Institution and director of the Wellcome Bureau of Scientific Research. His association with the laboratories, founded by the late Sir Henry Wellcome, has extended over thirty-six years. Dr. Charles H. Kellaway, F.R.S., director of the Walter and Eliza Hall Institute for Medical Research, Melbourne, will assume the directorship-in-chief of the institution and the foundation's other research laboratories as early in 1944 as possible. Dr. Wenyon has agreed to postpone his retirement until Dr. Kellaway reaches Britain. Dr. N. Hamilton Fairley, F.R.S., a director of medicine to the Australian Army in the Pacific, will eventually take over the directorship of the Wellcome Bureau of Scientific Research.

DR. IVOR GRIFFITH has been appointed research director of the Frank H. Lee Company, hat manufacturers, of Danbury, Conn. He will continue as dean of pharmacy at the Philadelphia College of Pharmacy and Science.

DONALD E. SHARP, formerly assistant to the vice-president and director of research of Hartford-Empire Company, of Hartford, Conn., has joined the Libbey-Owens-Ford Glass Company as assistant director in charge of glass technology.

DR. H. J. CHANNON, Johnston professor of biochemistry at the University of Liverpool, known for his work on fats and fat metabolism, has resigned to become associated with Unilever, Ltd.

MAJOR GENERAL JAMES C. MAGEE, a former Surgeon General of the Army, who has recently returned from a visit to the troops in England and North Africa, delivered on August 9 to the faculty and students of New York University College of Medicine a lecture on military medicine with special reference to tropical diseases.

THE Parsons Memorial lecture for 1943, given under the auspices of the Physical Society, London, will be delivered early in the autumn by Lord Rayleigh.

THE annual meeting of the American Psychological Association will be held at Northwestern University from August 31 to September 1. Owing to the serious crisis in the field of transportation it has been voted that council members only be encouraged to travel any distance to the annual meeting. Those in the immediate vicinity are invited to attend a "token" annual meeting. It is expected that most problems can be presented to the council by mail and that business requiring action can be handled by the emergency powers granted to the council at the last annual meeting if a quorum is not available. Other matters may need to be referred by mail to the broader base of associates and members. Headquarters will be maintained at Scott Hall. The council will be in session beginning on August 31 in the Hardy Lounge in Scott Hall. The "token" annual meeting is scheduled for Thursday, September 2, beginning at 1:30 P.M. in the auditorium of Lutkin Hall. It is expected that this meeting will be local and unrepresentative and that only those in the immediate vicinity whose presence will not tax the transportation system will attend.

The Times, London, reports that many leaders of British agriculture and representatives of twenty-eight nations gathered at Harpenden on July 27 to celebrate the centenary of Rothamsted Experimental Station. Welcoming the visitors at luncheon, Lord Radnor, chairman of the Lawes Agricultural Trust, said it was a matter of great pride to them that this was the first agricultural research station to celebrate its centenary. Lord Radnor paid a tribute to Sir John Russell, the retiring director. Mr. Hudson, congratulating Rothamsted on attaining its centenary, said "that phosphates had become the touchstone of agricultural production, and we owed the discovery of superphosphate to Sir John Lawes. Fortunately we were now receiving substantial imports of phosphate rock from North Africa, and this would be of great value in securing full crop output. Research was necessarily a long-term problem, and separate organization was needed to disseminate the fruits of research in practical knowledge among farmers." Sir John Russell expressed Rothamsted's pride in the world-wide recognition of the work of the past century.

AN expanded program of research through fellowship grants for the 1943–44 academic year has been announced by the Wm. S. Merrell Company, pharmaceutical manufacturers of Cincinnati. Research in

organic chemistry, bacteriology, pharmacology and biochemistry will be conducted at Cincinnati, Cornell, Illinois, Indiana, Louisville, Michigan, North Carolina, Ohio State, Pennsylvania and Temple Universities, and at Kansas State Teachers College. Grants for clinical research fellowships have been made to the Chicago Maternity Center, the University of Cincinnati, Harvard University, the University of Louisville, the University of Nebraska, the Pennsylvania Post-Graduate Hospital, Wayne University and Washington University.

Nature reports that the National Research Council of Canada will award for the academic year 1943–44 fourteen fellowships of the value of $750 each, thirty studentships of $650 each and twenty-one bursaries of $250 each. The sixty-five successful candidates for these post-graduate scholarships comprise graduates of fifteen Canadian universities, and they will carry out research work in the coming year at eleven of these institutions. As a result of war conditions, the fields of science in which the scholarship holders will work are reduced in number as compared with a few years ago. By far the greatest number will work in various branches of chemistry related to the war effort. According to a general classification adopted in announcing the awards, forty-nine will study chemistry, six physics (including one radiology), four biochemistry, two genetics, and one each biology, mineralogy, mechanical engineering and electrical engineering.

DISCUSSION

THE MOSSES OF LURAY CAVERN, VIRGINIA

THE writer returned[1] to the Caverns of Luray in the Shenandoah Valley of Virginia in September of 1941 for a more complete sampling of the mosses that are now growing upon the floor, walls and ceiling of the cavern wherever artificial light has been cast in time and amount sufficient to cause germination of the moss spores. Through the courteous assistance of the cavern management a thorough examination of the cavern was made, and all specimens which to the unpracticed eye appeared to be different in any form or color were collected. Though it can not be claimed that the collection is complete, it should present, however, a fair cross section of the kind of mosses in the Caverns of Luray. The specimens were sent to Dr. W. C. Steere, of the University of Michigan, who has kindly provided the identifications given in the column in Table 1 under "plant."

TABLE 1

Station	Plant	Description
Ramble	*Leptobryum pyriforme* (Hedw.) Schimp.	One-inch long thin stems, spare of leaves
Cross of 8	*Bryum pseudotriquetrum* (Hedw.) Schwaegr.	¾-inch long stems, well covered with leaves
Cross of 8, ground light	Moss—sp.?	2-inch long stems, luxurious leaf development
Mirror Lake	*Ceratodon purpureus* (Hedw.) Brid.	½-inch fine stems, small fine leaves
Entrance wall, 12 feet above floor	*Eurhynchium serrulatum* (Hedw.) Kindb.	Stems an inch or more long, quite leafy
Dream Lake	*Bryum pseudotriquetrum* (Hedw.) Schwaegr.	Long stems, leafy
	Weisia viridula (Hedw.)	Very short tight bunches of stems, leafy
	Thuidium sp.	Long stems full of tightly packed leaves
Ramble—ceiling	Algae	Minute filaments, fraction of mm long

[1] Walter B. Lang, SCIENCE, 94–2444, p. 414, October 31, 1941.

It is interesting to note that algae were found tenaciously growing to the limestone ceiling as a thin, compact, dark-green matte and under the same conditions as the mosses.

Supplemental samples of the moss specimens were spread between blotters and packed away at the time they were collected. When the containers were opened after the specimens had been more than a year without light or moisture they were found to be as green as ever.

Some two years ago the new Skyline Caverns near Front Royal, Va., were opened to the public after having been equipped with a modern lighting system. I was privileged at the time to make a thorough examination of the cavern for evidence of moss but found none except in the entrance corridor in the immediate vicinity of lights that are allowed to burn more or less continuously. This new moss growth appeared like a faint green fuzz upon the limestone. In time, it is expected that mosses will germinate within the cavern where the large projectors have been placed.

Dr. Frans Verdoorn has recently brought to my attention a paper by Jacques Maheu on American cavern flora[2] in which he presents some interesting conclusions regarding a comparison of American and European cave flora. Maheu states that the flora of Kentucky caves and those of Europe are the same and deduces therefrom that it is possible to establish one classification of cavern flora which will be universally applicable regardless of country or climate. He notes that American forms are more reduced and less varied, but that the variations are absolutely parallel with those of Europe; sterility, lengthening of the leaves, wider spacing of the leaves on the stems, elongation of the cells and disappearance or thinning of the nerve. The two most important factors in bringing about this

[2] La flore cavernicole américaine (Grottes de Mammoth-cave et de City-cave, état de Kentucky), *Bull. Soc. Bot. de France*, 63: 39–57, 1926.

transformation of plant life entering the environment of caves are humidity and reduction or total elimination of light. He further emphasizes the fact that of the American caves he has visited, he did not find the flora as rich as that of Europe and the neighboring species, but more transformed.

One wonders whether the flora in large caverns in the desert area of southwestern United States has not been more transformed where the humidity of the upper part of the cavern is affected by the regional environment.

WALTER B. LANG

U. S. GEOLOGICAL SURVEY

THE HEATH HEN

THIS is rather a belated attempt to draw attention to one of the statements made by Dr. W. C. Allee in his article published in SCIENCE for June 11 in which he cites safety in numbers as one of the evidences of natural cooperation. This is one of the most important principles of conservation and one which should be driven home to all Americans. I do not think there would be a better way to explode the idea that a single pair of animals can regenerate a host of the species than to quote from another publication of Dr. Allee's, "The Social Life of Animals," discussing the fate of the heath hen.

The heath hen was most abundant in Massachusetts, but by 1850 it had been killed off until it was to be found only on Martha's Vineyard and nearby islands and among the pine barrens of New Jersey. By 1890 to 1892 the birds had diminished to a scant two hundred at most, restricted to Martha's Vineyard. As soon as the "bird stuffers" heard how rare they had become, prices went up and museum collectors rushed in to get specimens before they disappeared like the dodo. By 1907 the count had been reduced to seventy-seven. The Heath Hen Association was formed. The society arranged for almost three thousand acres of protected range for the birds. By 1916 their numbers had increased to two thousand.

Then came a fire, a gale, and a hard winter, with an unprecedented flight of goshawks, and in April, 1917, there were fewer than fifty breeding pairs. The next year, when there was an estimated total population of one hundred and fifty, the heath hen range was invaded by several expert photographers who took motion pictures of mating behavior. In the face of this disturbance at a critical time, still a good year allowed the birds to increase and again spread over Martha's Vineyard. In 1920 three hundred and fourteen were counted; but thereafter a decline in numbers set in which was never stopped.

In spite of increased measures of protection, the census for the succeeding years were 117, 100, 28, 54, 25, 35. The last one seen was a banded male, in 1932. These facts clearly point out the folly of waiting until near extinction before preserving a species.

JAMES H. PANNELL

NUMBERING BOOK ILLUSTRATIONS

THE writers have a particularly good reason for agreeing *in toto* with the suggestions made in Lewis G. Westgate's article, "On Numbering Book Illustrations."[1] Eleven years ago we employed the principle now sponsored by Westgate of numbering tables and nomographs according to the page on which they occur.[2]

From the point of view of both author and publisher, more work is involved in numbering the table that is found on page 86 as Table 86. Comments we have received indicate that, from the reader's standpoint, this extra work is amply justified. We join with Westgate in hoping that an increasing number of authors will see that the figures, tables, etc., in their scientific texts and reference books are referred to by their page numbers.

ALBERT K. KURTZ

LIFE INSURANCE SALES RESEARCH BUREAU,
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JACK W. DUNLAP

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NEW WORDS IN SCIENCE

I WAS very much interested in a recent letter in SCIENCE by E. F. McDonald, Jr., discussing the new word, *Radionics*. As science editor of the College Standard Dictionary, now undergoing a thorough revision, it is a good part of my job to watch for, track down, estimate and define the hundreds of new terms being introduced into the various sciences, both theoretical and applied. Mr. McDonald's comments on *Radionics* sent me on a hunt through various current sources, but with disappointing results. I have not succeeded in finding the word in actual use in the few technical journals I have seen, including the *Review of Scientific Instruments*, *Science News Letter*, the *Journal of Chemical Education* and a number of recent books.

I wonder if any of your readers could supply me with further information on the origin, date of first use, originator, range of usage, etc., regarding this very expressive term? The status of the men who favor it over *electronics* (which I still find used rather extensively) suggests survival value and naturally I am anxious to see that it has the proper rating in our dictionary, along with a respectable number of other new terms, such as *vitamer*, *betatron*, *tectonophysics*, *paleopedology* and *geotechnology*.

It has long seemed to me that both scientist and layman would be greatly benefited by a more intelli-

[1] SCIENCE, 96: 581, December 25, 1942.

[2] J. W. Dunlap and A. K. Kurtz, "Handbook of Statistical Nomographs, Tables, and Formulas." World Book Company, vii + 163 pp. 1932.

gent and comprehensive treatment of what I like to call the language of science. Especially does this seem desirable in the general dictionary, as distinguished from the many technical glossaries accessible to—and often understood only by—trained specialists. In my personal files, as well as in the master files in the Funk and Wagnalls reference department, are hundreds of cards dealing with this field of knowledge alone. The material, indeed, is so rich, and it accumulates so rapidly, that I have been encouraged to compile a sort of annual glossary of new (or relatively new) scientific and technical terms, the first modest instalment of which appeared in the 1943 edition of the *New International Year Book*.

I hope that some of your readers with a flair for the terminology and nomenclature of the sciences may feel prompted to comment on the points raised in this letter, possibly even contributing such new terms as they consider important for the proper understanding of new developments in their own fields. It is true, as Faraday sensibly remarked, "that names are one thing and science another"—but was it not Faraday who gave us *electrolyte, anode, cathode, electrode, ion*? And, despite Mr. McDonald's plea for *radionics*, how large is the language-debt of science to Johnstone Stoney's fertile neologism, *electron!*

HAROLD WARD

NEW YORK, N. Y.

NATIONAL LEARNED SOCIETY GROUPS

IN my article "National Learned Society Groups" (SCIENCE, May 7), by some slip of the pen, I inadvertently mentioned the Geological Survey, intending to cite one of the Government Bureaus specifically mentioned before a House Committee by Secretary of the Interior Ickes. Actually the Survey is one of the few departments requiring of its staff, I am now told, a written statement of freedom from any paid connection with private corporate interests. I have been assured that this measure is strictly enforced, requiring rigid devotion in scientific matters connected with geology to the national interest. If all scientific departments of the nation and of the separate states, together with all colleges, universities and technical schools had this freedom from any private corporate connection my proposals would be superfluous.

Permit me to say that I have had scores of letters of approval and a score of interviews with supporters of my propositions; these include men in practically all the larger Eastern institutions as well as many in state universities, government bureaus and even from the far-off Oriental Institute of Oriental Studies in the Hebrew University of Jerusalem.

There have been four letters in opposition. I note that none of the objectors mention whether they have such paid connections with corporations.

LOUIS C. KARPINSKI

SCIENTIFIC BOOKS

SAMUEL F. B. MORSE

The American Leonardo. A Life of Samuel F. B. Morse. By CARLTON MABEE. 32 and 380 pp. New York: Alfred A. Knopf. 1943.

FROM the brilliant introduction by Professor Allan Nevins to the final of the 380 pages by the author the reviewer found this to be a highly interesting and informative book. The 1875 "official" biography by Prime (nearly 800 pages) is very largely filled with long letters by or to Morse and with copies of documents bearing on the story of the telegraph. But in this book the author has seized upon the salient points of many letters and documents even more than were known to Prime and, with occasional quotations, has painted a portrait rich in color, accurate in detail. Every important statement concerning Morse is documented; that is, a reference to the original source is given so that the reader may, if he wishes, verify its accuracy. These references (40 pages at the back of the book) number about 740, but one reference may contain a list of several sources so that the total number of documents to which the reader may refer runs into the thousands. However, there is unity, continuity, alluring appeal and literary excellence in the body of the book.

This is more than a biography of Morse; it is a story of his time. For here we get glimpses of many of the prominent men with whom Morse had contact: His father, the Reverend Dr. Jedediah Morse, the stern, just Congregational minister, the author of the first American geography, a founder of the American Board of Foreign Missions, projector of the Andover Seminary; the foremost painters Stuart, Copley, West, Trumbull; the foremost scientists Silliman, Day, James Freeman Dana, Oersted, Ohm, Henry, Wheatstone, Arago, Ampere; the writers, Coleridge, Bryant, Cooper; the inventors, Whitney, Fulton, Daguerre, Steinheil; the statesmen, President Monroe, many members of Congress, Lafayette. We follow Morse as a struggling painter with a great ambition to paint historical scenes but compelled by poverty to paint portraits, at times, 14 hours a day. In the book there are sixteen excellent reproductions

of paintings by Morse, chiefly portraits. They help to confirm the view, which many artists hold, that Morse was one of the foremost portrait painters of his time, comparing not unfavorably with Gilbert Stuart. We see Morse as a public-spirited citizen, a leader in the Nativist movement, a forlorn hope candidate for the mayoralty of New York. We note his fight against the O'Connel Guards, a military order of the Irish in New York, a forerunner of the German American Bund. We see him greeting the invention of the daguerreotype with great enthusiasm. He "saw in the image of a spider's head, no bigger than a pin, a minuteness of organization which he believed had not hitherto been known to exist. The discovery would open a new field of research, he predicted, with results as startling as when the microscope first came into use." He was one of the first American photographers. Then comes the great story of the beginning of the telegraph, and the Atlantic cable, the ridicule heaped by members of Congress on the idea of communicating intelligence through considerable distances by means of electric signals ("Senator Smith studied Morse's face for signs of insanity"), the successful experiment and the world's extravagant acclaim.

The author is critical in his appraisal of Morse as a scientist, but he gives a few quotations of the findings of scientific bodies. These make it clear that though Morse was not the sole inventor of the telegraph, he was the inventor of the Morse *method* of telegraphing—the method that has survived, with slight modifications, through these hundred years.

The reviewer has one mildly adverse criticism. It is in regard to the title. "Why drag in Velasquez?"—in this case, Leonardo? True, Morse called attention to the fact that artists may have abilities along various lines. He named Leonardo as a conspicuous example. Prime also names Leonardo as a scientist-artist, similar to Morse. But though there are points of similarity there are also great differences. Think of the origin of the two men. Think of Morse, the New England Puritan, the lifelong uncompromising foe of low standards in human conduct—then compare him with Leonardo. The author must share the view that there is an important difference, for there is probably more than mirth in his statement concerning Morse's friend and teacher, "Allston (a Southerner) was a Godfearing man, even compared with New Englanders." So where does Leonardo stand?

The book brilliantly bears out Professor Nevin's statement, "The life of Samuel F. B. Morse . . . is fascinating partly because of the versatility of his undertakings, partly because of the rich interest of his mind and character."

GORDON FERRIE HULL

ALASKA DIARY

Alaska Diary, 1926–1931. By ALEŠ HRDLIČKA. The Jaques Cattell Press, Lancaster, Pa. xv + 414 pp., with 232 illustrations. 1943. $5.00.

WERE it not for gas rationing and military priorities this book would precipitate a traffic jam on the Alaska highway. Dr. Hrdlička is careful to point out that there are other spots in the world for greater adventure, yet his clear style paints an intriguing picture of Alaska as offering the challenge of a frontier. The book is a diary of his archeological expeditions to Alaska, Yukon, Kuskokwim River and Nushagak, but it tells far more than the mere recovery of stone tools and human bones. It tells much of the living people of Alaska; it tells of the weather, of food, of transportation; it tells of opportunities, of hardships; and always it tells of Alaska, our far northwest border-country. Dr. Hrdlička went on these expeditions not as an "adventurer" or "explorer," but as a trained observer seeking to learn more of natural laws, especially as related to man and his prehistory. The volume is not an epic with pretense to literary grandeur; it is the day-by-day record of a simple unassuming man who looked, listened and stopped to learn.

On the expeditions Dr. Hrdlička collected nearly 4,000 crania and skeletons and measured many living. From the study of these data he concluded that "the entire littoral region of northwestern Alaska north of the Yukon, the habitable islands of the Bering Sea and the lower portions of the three large rivers appear to have always been occupied by the Eskimo." No trace of any other type of man has been found here. The upper reaches of the Yukon, the Kuskokwim and Nushagak were always sparsely occupied by Indians.

The Eskimos are not homogeneous, probably traceable to "a number of strains" in Asia. Three subtypes are recognized among the Indians: (1) the Yukon, Tananá and upper Kuskokwim; (2) Shageluk-Slough; (3) the Chugatchi to the south of the Nushagak. There are no distinct lines of demarcation between Eskimo and Indian types, although extremes in each are readily distinguishable, one from the other.

Dr. Hrdlička concludes that no mass migration came over from Asia. Rather, "the Asiatics came in dribbles," along the coast and a bit inward at river mouths. As to the time element, he concludes that "it could not be called very ancient, not reaching perhaps beyond the earlier parts of our era."

The publishers are to be congratulated upon their technical skill. The book is printed upon excellent paper and the illustrations, mostly photographs by the author, often taken under adverse lighting condi-

tions, are well reproduced. The author is to be congratulated upon a fascinating record of scientific observation. It probably won't rank with the "Voyage of the Beagle" in importance, but it certainly evidences the same motivation of intellectual and scientific curiosity.

WILTON MARION KROGMAN
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TIMBER

Timbers of the New World. By SAMUEL J. RECORD and ROBERT W. HESS. xv + 640 pp., 58 plates, 75 figs., 8 maps. New Haven: Yale University Press. 1943. $10.00.

"TIMBERS of the New World" is the successor to but not a second edition of "Timbers of Tropical America," published in 1924. The new work contains more than twice the amount of material as in the old and is treated differently. In the old work a detailed macroscopic description is given for each individual wood with very little anatomy. Since the publication of "Timbers of Tropical America," Record and Hess and other investigators interested in the comparative anatomy of wood have devoted more time to detailed anatomy. However, in order to limit the descriptions of so many woods to one volume, the old plan could not be adopted for the new work because its field is extended to include species north and south of the tropics of the entire Western Hemisphere. This is the first attempt by any one to deal with all the larger woody plants of the Americas.

The new work is an encyclopedia of the best information available concerning the trees and larger shrubs native to South America, Central America, Mexico, the West Indies, U. S. A. and Canada. There are descriptions of the trees and woods of more than 1,100 genera and 155 natural families. For convenience of the reader the arrangement is alphabetical by families and genera. Under each family is listed the number of genera and species, their geographic location and a general description of flowers, leaves and fruit. The genera of greatest economic importance are emphasized. There follows a general macroscopic description of the woods. In fine print is given a detailed anatomical description of the family by genera followed by a reference such as that given for the Anacardiaceae: "For anatomy of the different genera see Tropical Woods 60: 16–45." Following the anatomical description of the woods of the family the various genera are listed alphabetically. Under each genus are given the important economic species with descriptions of the tree, flowers, fruits and leaves, and a macroscopic generic description of the woods. The important economic products such as drugs, oils, resins, fruits, etc., together with the uses of the woods are listed for each species. At the end of each generic account is given an alphabetical list of trade and common names for the woods by countries.

The latest accepted terminology is used doing away with much confusion which existed concerning the nomenclature of certain genera, such as: *Tecoma* and *Tabebuia* in the Bignoniaceae; certain species of *Cordia* in the Boraginaceae; *Amburana* and *Torresia*, *Cajoba* and *Pithecolobium*, *Libidibia* and *Caesalpinia*, *Vatairea*, *Andira* and *Tipuana* of the Leguminosae. Other examples could be mentioned. Furthermore, the botanical identities of timbers which have been known to commerce for a long time, such as Cocobolo, the Rosewoods, Brazil wood, Kingwood, etc., have been cleared up.

In recent years certain investigators have attempted to correlate anatomical characters of the stem with gross morphological characters in a natural system of classification. Toward this end the results obtained from anatomical studies, approached from the point of view of phylogeny, have given striking results. The authors state in the preface:

> Taxonomic botanists base their concepts of families, genera, and species on morphological characters of the reproductive and vegetative parts of a plant, and are not always in agreement as to the constitution of particular groups. . . . The present authors have considered these taxonomic problems from the standpoint of wood anatomy, and when confronted with alternative proposals by different botanists, have made their choice on the basis of anatomical characteristics.

As an example, the species of *Picrodendron* have been variously referred to the Juglandaceae, Anacardiaceae, Sapindaceae and Simarubaceae, are similar in wood structure, and do not indicate close affinity to any of the four families to which the genus has been referred. The genus, therefore, has been placed in the family Picrodendraceae established by Small in 1917. Several other examples concerning inconsistencies in current classification are called to the attention of specialists in those groups.

Toward the end of the book is an explanation of the terms used in the wood descriptions. The terms are illustrated with 75 excellent photomicrographs prepared especially to show variety of anatomical details. Also at the end of the book are lists of families classified with reference to special properties and uses of their bark, leaves and timber. The special lists are designed for convenience in locating trees and woods having special properties and uses or suitable for the same purposes as better-known kinds. The wood descriptions are based upon specimens in the collections of the Yale School of Forestry. The total number of samples available for comparative study is about 40,600, of which 22,000 are American. At the end is a complete bibliography of the principal publications arranged by countries.

The book is indispensable as a general reference for taxonomists, teachers and students of economic botany and wood technology, and others who are interested in the economic products of the forest, including wood utilization.

DAVID A. KRIBS

SOCIETIES AND MEETINGS

THE ANNUAL MEETING OF THE ROYAL SOCIETY OF CANADA

THE annual meeting of the Royal Society of Canada was held at McMaster University, from May 25 to 27. The scientific sections of the society held their meetings in the Science Building of the university and the general meetings took place in Convocation Hall. The president of the society, Professor J. B. Collip, F.R.S., presented the medals at the evening meeting on May 25. The Flavelle medal was awarded to Professor B. P. Babkin for his outstanding work in analyzing the secretory mechanism of the digestive glands. Professor John L. Synge received the first award of the Henry Marshall Tory medal for outstanding contributions to applied mathematics, and the Willet G. Miller medal, also awarded for the first time, was presented to Professor Norman Levi Bowen in recognition of his contributions to geology. Following the presentation of the medals, Dr. Collip read his presidential address on "Science and War." After briefly reviewing the part played by science in former conflicts, Dr. Collip emphasized the important contributions of physicists, chemists and other scientists in the present war. He dealt in some detail with aviation medicine and the cooperation between the men of science and the armed forces in solving many of the problems which modern warfare presented. He referred to the recognition and support that scientists were now receiving as an integral part of the war effort and pointed out that much of this research work is producing results that will be equally important in the post-war period.

A further feature of the meeting was the symposium, held after the dinner on May 26, on "Medical Investigations as Applicable to the Armed Forces," at which Surgeon Captain A. McCallum, Medical Director General of the Royal Canadian Navy, spoke in general terms of the organization for research in this service and of the work already accomplished. Surgeon Commander C. H. Best, F.R.S., director of the Royal Canadian Naval Medical Research Unit, gave a more detailed account of some of the results achieved in connection with nutrition, night-vision and similar problems. Brigadier J. C. Meakins outlined briefly the medical research going on in the army and Group Captain J. W. Tice, director of Medical Services (Air), spoke of some problems of interest to the Air Force in particular. This was followed by Squadron Leader K. A. Evelyn, who discussed in further detail many of the special problems in aviation medicine, at the conclusion of which he showed a moving picture film entitled "Oxygen." This film was shown as a special feature, permission for which had been specially granted. The film was prepared under the auspices of the Associate Committee on Medical Research of the National Research Council for use in training enlisted aircrew in the essentials of physiology and the effects of high altitude flying, pointing out the importance of the special precautions required.

Professor J. K. Robertson delivered the presidential address in Section III (Chemical, Mathematical and Physical Sciences) on "The Role of Physical Optics in Research," in which the speaker reviewed the discoveries into the nature of light, atomic and molecular structure and in astronomy that have resulted from the application of physical optics in spectroscopy, interferometry and diffraction. This historical account was followed by an address on "Chemical Reactions of Excited Atoms," by Dr. E. W. R. Steacie, and a paper on "Molecular Spectra and their Applications," by Dr. Andrew McKellar, who spoke particularly of applications in astronomy. Thirty-eight papers were presented to the section, the majority of which were read by title. Owing to the pressure of war work few physicists and chemists were in attendance, but mathematics and astronomy were well represented. Among those papers which were read, mention may be made of a few of some general interest. Professor Lachland Gilchrist and J. W. Britton gave an account of further experiments on the use of drill holes in electrical methods as an aid to the location of mineralized bodies and rock structure. Dr. J. A. Pearce announced the orbital elements of H.D. 222107 lambda Andromedae as revised on the basis of recent measurements and also the orbital elements of the spectrographic Binary H.D. 34333. A paper of particular interest was given by Dr. L. M. Pidgeon on the production of light metals, in which he reviewed the methods for the separation of magnesium and the difficulties which had to be overcome. He gave an account of his own experiments which resulted in the present method used in obtaining large quantities of magnesium metal in Canada since the outbreak of hostilities. Dr. H. F. Manske and L. Marion reported the isolation of eight alkaloids from *Lycopodium annotium* L. Several papers were presented by Dr. Paul E. Gagnon and

his co-workers, among which mention may be made of one in which the isolation of some new sulfamides in the 1-1-Diphenylindane was announced. Perhaps the most interesting paper presented to the section was one of those given by Professor E. F. Burton, in which J. H. L. Watson showed how stereoscopic photographs had been taken with the electron microscope and exhibited several examples to the members present. This new technique enables one to view the objects photographed so as to bring them out in three dimensions, thus adding depth to the pictures and revealing new features in the structure of smoke and metallic particles. At the conclusion of the sectional meetings, Professor T. Thorvaldson was elected president of the section for the year 1943–44.

In Section IV (Geological Sciences), Professor M. B. Baker gave the presidential address and spoke on "Gold and Iron Prospects in Canada." This address was followed by sixteen papers on various geological investigations. Among these Dr. E. A. Hodgson delivered a very interesting paper on the "Rock Burst Experiments at Lake Shore Mines, Kirkland Lake." The author outlined the program of the investigations carried out since 1939 and gave some of the results already obtained. Equipment has been designed to pick up, amplify and record the small subaudible snaps which occur in a rock under pressure and which increase in number as the pressure increases. The records of a severe rock burst which occurred on January 29, 1943, show conclusively that the method clearly delimits the area under pressure to within a hundred feet or less. So far, attempts to predict bursts as to time have not been successful; but it is hoped that further work will result in some measure of time prediction.

Professor G. B. Reed, president of Section V (Biological Sciences), spoke on "Wound Infections and Local Chemotherapy." This paper dealt with the treatment of wounds with the sulfa drugs and the speaker emphasized the necessity of applying the drug as soon as possible after the wound has been inflicted in order to obtain the greatest benefit. Fifty-six papers were presented to this section, many of which will appear in scientific journals. Space permits the mention of the two invited papers only. The one by Dr. Babkin, on "Secretory Mechanism of the Digestive Glands," contained a survey of the work of his laboratory on this subject. Briefly it might be stated that the investigations established that the mucous, demilune and myo-epithelial cell groups of the submaxillary gland each have a separate innervation, and that the surface epithelium cells of the gastric mucosa and the mucoid, peptic and parietal cells of the gastric glands are under independent nervous or humoral control. The conclusions to be derived from this work were stated and further analysis of the secretory function of the digestive glands given. The second paper, by Professor G. W. Scarth, on "The Mechanism of Frost Resistance," contained an account of the modes of frost injury to plant cells and of the protoplasmic changes which accompany frost-hardening. He also discussed how the different hardening changes afford protection. The new president of this section is Professor H. S. Jackson.

At the general meeting of the society, Monsignor Olivier Maurault, rector of the University of Montreal and a fellow of Section I, was elected president of the Royal Society of Canada and Professor J. K. Robertson was elected vice-president.

DAVID A. KEYS

SPECIAL ARTICLES

THE PRODUCTION OF FOLIC ACID BY RAT LIVER IN VITRO

A PRELIMINARY study,[1] using *Streptococcus lactis R*, indicated that the urine of man contains only very small amounts of folic acid. We have found, using *Lactobacillus casei*, that the daily urinary excretion of this factor by 15 normal individuals, based on the assay of 42 samples, averages 0.0108 mgm units (0.0038 to 0.0238 mgm units).[2] The average daily folic acid intake of well-fed adults has been reported to be about 1.4 mgm units per day.[3] Evidently folic acid is unlike other members of the vitamin B complex (thiamine, riboflavin, pantothenic acid, biotin) in that only a trace appears in the urine of man (< 1 per cent. of the probable dietary intake).

To test the possibility that the folic acid is excreted in the urine in a complex form without microbiological activity, urine samples were subjected to autoclaving, autoclaving with very dilute acid or alkali, and digestion with takadiastase (an enzyme preparation used to release folic acid from tissue combination[2]). These procedures did not increase the amount of folic acid found in the urine. We have observed, however, that incubation of urine with a fresh rat liver preparation causes the appearance of more folic acid than can be accounted for by the analysis of the constituents of the digestion mixture. In conducting such experi-

[1] L. D. Wright, J. R. McMahan, V. H. Cheldelin, A. Taylor, E. E. Snell and R. J. Williams, University of Texas Publication, 4137: 38, 1941.
[2] V. H. Cheldelin, M. A. Eppright, E. E. Snell, B. M. Guirard, University of Texas Publication, 4237: 15, 1942.
[3] R. J. Williams, *Jour. Am. Med. Asn.*, 119: 1, 1942.

ments we have usually employed 10 cc of urine, or of other test materials dissolved in water, to which has been added 10 cc of a 20 per cent. suspension of fresh rat liver (2 parts of liver ground in a Waring blendor with 8 parts of M/10 phosphate buffer, pH 7). In some experiments we have used a weighed sample of liver fragmented in phosphate buffer with a spatula. Takadiastase (0.4 per cent.) is added, but this does not participate in the formation of folic acid by the liver preparation, under the influence of added substances. The mixtures are covered with a thin layer of benzene and allowed to incubate at 37° C. for 18 to 24 hours. After incubation folic acid is determined in the tissue filtrates by microbiological methods.[4]

Using the technics described we have investigated the material present in urine and the conditions requisite to the formation of folic acid by the rat liver preparation. No increase in the folic acid content occurs, over that calculated from the analyses of the constituents, if a heated rat liver preparation is used. The reaction is inhibited by high concentrations of NaCl and by M/500 NaCN and does not occur if liver extracts are used instead of fresh rat liver. The material in urine is stable to autoclaving for 1½ hours in the presence of normal HCl or H_2SO_4, under which circumstances folic acid itself is destroyed. The substance is readily absorbed on fullers' earth[5] at pH 3 and may be eluted with ammoniacal 50 per cent. alcohol. Using such procedures the material in urine has been concentrated approximately 2,000 times. When other natural materials (grass and liver extracts) are autoclaved with acid and then incubated with liver tissue, more folic acid is usually found on assay of the filtrates than can be accounted for by the analyses of the materials tested.

The stability to acid and the adsorption-elution characteristics of the substance in urine suggest that it may be related to uropterin (a urinary pigment),[6] or xanthopterin (the pigment of yellow butterfly wings),[7] which is claimed to be identical with uropterin.[6] When synthetic xanthopterin[8] is incubated with liver tissue a significant increase in the folic acid content of the filtrate from the mixture is usually found. This increase may be demonstrated with either *L. casei* or *Strep. lactis*. Before incubation with rat liver xanthopterin is entirely ineffective in replacing folic acid as a growth factor for either organism. Xanthopterin alone, among the pure compounds thus far tested, causes the formation of an increased amount of folic acid when incubated with rat liver. The following substances have been found ineffective: adenine, guanine, xanthine, uracil, cytosine and synthetic leucopterin[8] (the pigment of white butterfly wings[7]).

Preliminary evidence indicates that under certain circumstances the yield of folic acid, obtained by incubating liver with superfiltrol-eluates from acid-autoclaved liver extracts, may be materially increased by the addition to such mixtures of an aqueous extract of an acid ether extract of acid-autoclaved liver. Such an extract contains a considerable amount of acidic organic material, but is, of course, devoid of folic acid. An attempt to identify the substance or substances responsible for the effect of this material is now in progress. It is possible that the yields of folic acid obtained, when the xanthopterin-like material in acid-autoclaved liver extracts is incubated with rat liver, are limited by the supply of substances related to those found in the ether soluble fraction.

Discussion

Our experiments indicate that a substance stable to both heat and normal acid occurs in either free or combined form in urine, grass and liver. It appears likely that in some materials (grass) a considerable portion of this substance is derived from the degradation of folic acid, in other materials (urine and some liver extracts) the amount formed by autoclaving with acid is too large to have been derived from folic acid alone. The substance, when incubated with a preparation of fresh rat liver, causes the formation of folic acid; an effect also produced by synthetic xanthopterin. The substance obtained from urine, grass and liver has not yet been identified; however, the evidence suggests that it is related to xanthopterin.

Mitchell[9] has claimed that xanthopterin occurs in folic acid concentrates, and Totter and Day[10] have reported that xanthopterin, like concentrates of folic acid, promotes growth and cures leucopenia in rats fed succinylsulfathiazole in highly purified rations. Although neither we nor others[11] have been able to confirm this finding with xanthopterin, we believe a possible explanation of the conflicting data may be based on our results. A personal communication from Dr. Day suggests that age or duration of feeding the purified diet might be involved. It is possible that the response obtained from xanthopterin in rats may be limited by the availability of another substance. Such a possibility is suggested by the results we have obtained with material extracted by ether from a liver

[4] M. Landy and D. M. Dicken, *Jour. Lab. and Clin. Med.*, 27: 1086, 1942.
[5] Superfiltrol (thiamine grade).
[6] W. Koschara, *Zeit. f. physiol. Chem.*, 240: 127, 1936.
[7] C. Schöpf and E. Becker, *Ann.*, 507: 266, 1933.
[8] The syntheses of xanthopterin and leucopterin were generously carried out by our colleagues, Drs. A. M. Land and J. M. Sprague, according to the methods of R. Purrmann, *Ann.*, 544: 182, 1940 and 546: 98, 1940.
[9] H. K. Mitchell, SCIENCE, 97: 442, 1943.
[10] J. R. Totter and P. L. Day, *Jour. Biol. Chem.*, 147: 257, 1943.
[11] Personal communication from several laboratories.

TABLE 1

THE FOLIC ACID CONTENT OF RAT LIVER AFTER INCUBATION WITH VARIOUS SUPPLEMENTS

Expt. No.	Incubation mixture (Liver plus Supplement)	Folic Acid Content per gram of		Folic Acid formed per gram of liver
		Liver alone	Liver plus Supplement	
		μ gm units*	μ gm units*	μ gm units*
1	Liver (2.0 gm) + Urine (10 cc = 0.08 μ gm units of folic acid)	9.2	17.2	8.0
2	Liver (2.0 gm) + Urine (10 cc = 0.08 μ gm units of folic acid)	16.0	26.0	10.0
3	Liver (4.8 gm) + Urine (20 cc = 0.16 μ gm units of folic acid)	10.0	30.8	20.8
4	Liver (3.0 gm) + Urine (10 cc)	6.8	12.8	6.0
	Liver (3.0 gm) + Urine (10 cc) after treatment with superfiltrol	6.8	8.8	2.0
	Liver (3.6 gm) + Superfiltrol eluate ≅ 10 cc urine	6.8	12.9	6.1
5	Liver (2.5 gm) + Urine (10 cc = 0.13 μ gm units of folic acid)	10.4	14.4	4.0
	Liver (2.1 gm) + Acid-autoclaved urine (10 cc = 0.00 μ gm units of folic acid)	10.4	23.2	12.8
6	Liver (2.0 gm) + Xanthopterin (250 μ gm)	8.0	14.0	6.0
7	Liver (2.0 gm) + Xanthopterin (250 μ gm)	5.6	17.2	11.6
8	Liver (2.0 gm) + Xanthopterin (250 μ gm)	4.0	10.4	6.4
9	Liver (2.0 gm) + Adenine, guanine, xanthine, uracil or cytosine (250 μ gm)	4.4–4.8	4.4–4.8	0.0
	Liver (2.0 gm) + Xanthopterin (250 μ gm)	4.6	15.2	10.6
10	Liver (2.0 gm) + Leucopterin (250 μ gm)	16.0	14.4	0.0
11	Liver (2.9 gm) + Armour's parenteral liver extract (15 anti-P.A. units per cc) (0.1 cc = 1.4 μ gm units of folic acid)	20.0	26.0	6.0
12	Liver (2.6 gm) + Powdered Liver Concentrate (Wilson's 1 : 20), 200 mgm = 3.0 μ gm units of folic acid per gram of rat liver present	8.4	11.2	2.8
	Liver (3.1 gm) + Acid-autoclaved Powdered Liver Concentrate (Wilson's 1 : 20), 200 mgm = 0.02 μ gm units of folic acid per gram of rat liver present	8.4	36.4	28.0

* Results are expressed in terms of μ gm "potency 40,000 material," as described by V. H. Cheldelin, *et al.* (footnote 2).

extract autoclaved with acid. Such a substance might be stored to some extent in the liver of rats on normal diets, and might be derived from either dietary sources or from bacterial synthesis in the intestine. With continued feeding of purified diets or of purified diets containing succinylsulfathiazole, liver storage would be progressively reduced and the influence of xanthopterin on the synthesis of adequate amounts of folic acid in the liver of the rat would be inhibited.

Xanthopterin has been reported as effective in the cure of goats' milk anemia in rats[12] and as an anti-anemia factor for fish.[13] Evidence has recently been presented which indicates the identity of folic acid with a crystalline chick anti-anemia factor (vitamin B_c),[14] which has enormous activity as a growth factor for *L. casei* in the absence of folic acid concentrates,[14] and which functions similarly for *Strep. lactis.* Concentrates containing folic acid have proved effective in the treatment of leucopenia and anemia in the rat on purified diets containing poorly absorbed sulfonamides,[15, 16] and in the monkey on purified diets alone.[17, 18] In one monkey alleviation of leucopenia and anemia followed the use of xanthopterin when a liver powder prepared by heating fresh liver at 100° C. for 24 hours was also fed. Neither substance was effective by itself.[19]

It appears reasonable to suggest that from xanthopterin or closely related compounds may be derived substances concerned with the formation of erythrocytes and granulocytes. Various animal species appear to vary in the complexity of their requirements for hemocytopoietic material. In man the utilization of dietary anti-anemia material (extrinsic factor) is known to require the participation of an additional substance found in gastric juice (intrinsic factor), for the formation of what appears to be a more complex

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substance (anti-pernicious anemia factor). Assays of several liver extracts intended for parenteral use in pernicious anemia therapy have shown the presence of small amounts of folic acid, and of larger amounts of the substance(s) formed by autoclaving with acid.

SUMMARY

The occurrence in urine and in acid-autoclaved grass and liver extracts of a substance which appears to participate in the synthesis of folic acid by rat liver *in vitro* is described. A similar effect is produced by synthetic xanthopterin. The effect of these materials might be accomplished by (1) catalysis of the enzymatic synthesis of folic acid; (2) the release of folic acid not liberated by takadiastase from tissue complexes; or (3) their serving as substrate material for the enzymatic synthesis of folic acid. The data presented favor the last hypothesis and suggest that xanthopterin, or a substance derived from it, may constitute a portion of the folic acid molecule. The probable involvement of compounds related to xanthopterin in the formation of hemocytopoietic substances in several animal species is discussed.[20]

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DISTRIBUTION AND HEREDITY OF VARIANTS OF THE RH TYPE[1]

WITH the aid of anti-rhesus immune sera, Landsteiner and Wiener[2] divided human beings into two classes, Rh positive and Rh negative, the former comprising about 84 per cent. of white individuals in New York City. These authors[3] also showed that the Rh factor is inherited as a simple mendelian dominant, independently of the blood groups and M-N types. The Rh factor has proved to be of considerable clinical importance in the etiology of intragroup hemolytic transfusion reactions[4,5] and in the pathogenesis of erythroblastosis fetalis.[6,7,8]

It was early recognized that the Rh factor is antigenically and genetically complex. Thus, Wiener[5] described an anti-Rh serum which agglutinated only about 70 per cent. of all bloods from white individuals, and pointed out that with the aid of this special anti-Rh serum the Rh type can be subdivided into two subtypes analogous to the major subgroups of A. According to the terminology suggested by Wiener and Landsteiner,[9] Rh positive bloods reacting with the special anti-Rh serum (now designated anti-Rh_1) belong to type Rh_1, while the remainder (about one sixth of the Rh positive bloods) belong to type Rh_2. As Wiener and Landsteiner[9] have shown, the types Rh_1, Rh_2 and negative are inherited by means of triple allelic genes Rh_1, Rh_2 and rh, where Rh_1 and Rh_2 are both dominant over rh and and Rh_1 is dominant over Rh_2.

The situation is further complicated by the fact that some bloods of subtype Rh_1 (reacting with anti-Rh_1 serum) do not react with guinea-pig anti-rhesus serum, so that a fourth type is determined in that way.[3] This type (designated as Rh′) is rare, comprising only about 3 per cent. of all white individuals. It should be mentioned that to allow for this special type, it was originally suggested that the standard guinea-pig anti-rhesus (giving about 84 per cent. positive reactions) be designated as anti-Rh_1, and the anti-Rh serum giving 70 per cent. positive reactions as anti-Rh_2.[10] This terminology has been abandoned, however, because it was found that the hypothetical agglutinogens determined in this way do not mendelize like A and B but are apparently "partial antigens" like the factors B_1, B_{11}, B_{111} . . . of human group B blood, and the factors F_A, A_1, A of group A_1 blood.[11] In the present communication, only the major subtypes, Rh_1 and Rh_2, and not type Rh′, will be included in the discussion.

Recently, Wiener and Sonn[12] have described a serum from a mother of an erythroblastotic infant, which contained a potent anti-Rh agglutinin reacting

20 We are indebted to Miss Helen Ryan for capable assistance; to Dr. W. R. Graham, of the Cerophyl Laboratories, for generous supplies of grass juice powder; to Dr. David Klein, of the Wilson Laboratories, for the powdered liver concentrate (1 : 20). Some of the data in this paper were presented before the Philadelphia Physiological Society on May 18, 1943; an abstract appears in the *Am. Jour. Med. Sci.*, 206: 128, 1943.

1 From the Serological Laboratory of the Office of the Chief Medical Examiner of New York City. Aided by a grant from the Carnegie Foundation and the Committee on Human Heredity of the National Research Council.

2 K. Landsteiner and A. S. Wiener, *Proc. Soc. Exp. Biol. and Med.*, 43: 223, 1940.

3 K. Landsteiner and A. S. Wiener, *Jour. Exp. Med.*, 74: 309, 1941.

4 A. S. Wiener and H. R. Peters, *Ann. Int. Med.*, 13: 2306, 1940.

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6 P. Levine, E. M. Katzin and L. Burnham, *Jour. Am. Med. Assoc.*, 116: 825, 1941.

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9 A. S. Wiener and K. Landsteiner, *Proc. Soc. Exp. Biol. and Med.*, 53: 167, 1943.

10 As was first shown by Levine, and confirmed by Wiener, the most common human anti-Rh sera, now designated anti-Rh′, giving about 87 per cent. positive reactions, contain two agglutinins, one corresponding to the 84 per cent. sera (anti-Rh), the other to the 70 per cent. sera (anti-Rh_1).

11 A. S. Wiener, "Blood Groups and Transfusion," 3rd edition, p. 254. Springfield, Ill.: C. C Thomas. 1943.

12 A. S. Wiener and E. B. Sonn, *Jour. Immunol.*, in press.

with only about 30 per cent. of bloods of white individuals. The agglutinogen detected by this serum appears to be of clinical importance in relation to the occurrence of hemolytic reactions in certain Rh positive patients and in many cases of erythroblastosis.[13] Wiener and Sonn[12] have shown that the agglutinogen detected by the new anti-Rh serum is inherited as a simple Mendelian dominant, probably by means of a special allelic gene. Therefore, these observations may also have application in forensic medicine, not only by further increasing the identifiable types of human blood but also by substantially increasing the chances of exclusion in cases of disputed parentage. The purpose of the present communication is to present some new data on the distribution of the major variants of the Rh type, which are of significance in relation to the heredity mechanism.

The Rh reactions of a random series of 280 blood samples from white individuals in New York City are summarized in Table I. It is evident that the

TABLE I

DISTRIBUTION OF THE SUBTYPES OF RH

Type*	Rh_1		Rh_2		Negative		Total
Reaction with special anti-Rh serum	Pos.	Neg.	Pos.	Neg.	Pos.	Neg.	
Number	49	141	35	16	1	38	280
Per cent.	17.5	50.3	12.5	5.8	0.3	13.6	100.0
Number in major types	190		51		39		280
Per cent.	67.8		18.3		13.9		100.0

* Determined with the aid of human anti-Rh′ and anti-Rh_1 sera.

new anti-Rh serum makes possible further subdivisions within the major subtypes Rh_1 and Rh_2 and that the incidence of positive reactions is much higher in the latter type. For this and other reasons (see below), it is proposed tentatively to designate the new agglutinin as anti-Rh_2 and the agglutinogen detected by it as Rh_2. Thus, type Rh_1 is now subdivided into type Rh_1Rh_2 (positive with anti-Rh_2 serum) and type Rh_1 proper (negative with anti-Rh_2 serum), while type Rh_2 is subdivided into type Rh_2 proper (positive with anti-Rh_2 serum) and Rh (negative with anti-Rh_2 serum). In the so-called Rh-negative type, there are rare bloods agglutinated by the anti-Rh_2 serum (see Table I). It is obvious that such individuals should now be deleted from the Rh negative type, because the use of their blood for patients actively or passively sensitized to the Rh_2 agglutinogen might prove dangerous.

The hypothesis that the agglutinogen detected by the anti-Rh_2 serum is determined by a gene allelic to *rh* can be tested as follows:

[13] A. S. Wiener, *Amer. Jour. Clin. Path.*, in press.

If we disregard the reactions of the anti-Rh_2 serum, the distribution of the major subtypes in our series is as follows:

$$\text{Type } Rh_1 = 67.8 \text{ per cent.} \quad (1)$$
$$\text{Type } Rh_2 = 18.3 \text{ per cent.} \quad (2)$$
$$\text{Rh negative} = 13.9 \text{ per cent.} \quad (3)$$

and the frequencies of the three corresponding genes are calculated in the usual manner:[14]

$$rh = \sqrt{\text{Neg.}} = \sqrt{0.139} = 37.3 \text{ per cent.} \quad (4)$$
$$Rh_2 = \sqrt{\text{Neg.} + \text{Rh}_2} - \sqrt{\text{Neg.}} = 19.5 \text{ per cent.} \quad (5)$$
$$Rh_1 = 1 - (rh + Rh_2) = 43.2 \text{ per cent.} \quad (6)$$

If, on the other hand, we only take into account the reactions of the anti-Rh_1 and anti-Rh_2 sera and disregard the anti-Rh′ serum, four types are distinguished as follows:

$$\text{Type } Rh_1Rh_2 = 17.5 \text{ per cent.} \quad (7)$$
$$\text{Type } Rh_1 = 50.3 \text{ per cent.} \quad (8)$$
$$\text{Type } Rh_2 = 12.8 \text{ per cent.} \quad (9)$$
$$\text{Negative} = 19.4 \text{ per cent.} \quad (10)$$

The possibility that the agglutinogens detected by the anti-Rh_1 and anti-Rh_2 sera are independent of each other is immediately excluded because $Rh_1 \times Rh_2$ is almost twice as great as $\text{Neg.} \times Rh_1Rh_2$. On the other hand, the hypothesis that the agglutinogens detected by the sera anti-Rh_1 and anti-Rh_2 are determined by corresponding allelic genes Rh_1 and Rh_2 can be tested by calculating the frequencies of the hypothetical genes from the distribution of the four classes above and determining whether the sum of the frequencies equals unity (or 100 per cent.):[15]

$$rh^{16} = \sqrt{\text{Neg.}} = \sqrt{0.194} = 44.5 \text{ per cent.} \quad (11)$$
$$Rh_1 = \sqrt{\text{Neg.} + \text{Rh}_1} - \sqrt{\text{Neg.}} = 39.0 \text{ per cent.} \quad (12)$$
$$Rh_2 = \sqrt{\text{Neg.} + \text{Rh}_2} - \sqrt{\text{Neg.}} = 12.0 \text{ per cent.} \quad (13)$$
$$rh + Rh_1 + Rh_2 = 95.5 \text{ per cent.} \quad (14)$$

The agreement between the calculated and expected results is not entirely satisfactory, but this may be due in part to the relatively small size of the series, and perhaps more probably to difficulties with the technique of these delicate tests. The expected frequency of type Rh_1Rh_2 equals $2 \times Rh_1 \times Rh_2$ or 9.4 per cent.; *i.e.*, much less than the observed frequency. This suggests that the problem be further investigated, concentrating particularly on bloods of this type. Of course, additional family studies will also aid in the solution of the problem.

In conclusion, it may be mentioned that the existence of variants of Rh serves to explain the puzzling observations on the differences in specificity of human

[14] *Cf.* A. S. Wiener, "Blood Groups and Transfusion," p. 215, 1943.

[15] *Cf.* A. S. Wiener, "Blood Groups and Transfusion," p. 186, 1943.

[16] This value is greater than that given in (4) because some Rh_2 bloods are now included in the "negative" class. For the same reason, the value given by (13) is less than that given by (5).

anti-Rh sera. Thus, it is now possible to anticipate the behavior of a post-transfusion anti-Rh serum if the Rh subtype of the donor is known, while the quality of the anti-Rh agglutinins in sera from mothers of erythroblastotic babies may be predicted by tests on the blood of the husband or infant.[17] On the other hand, the uniformity in specificity of the guinea-pig antisera is most likely due to the corresponding uniformity of the Rh-like antigens in the red cells of different rhesus monkeys.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

THE DEMONSTRATION OF THE PROTOZOAN PARASITE OF QUAIL MALARIA BY FLUORESCENCE MICROSCOPY

THE favorable results which have been obtained in development of diagnostic methods for detecting acid-fast bacteria by fluorescence[1] (Hagemann and others) and the results obtained by Bock and Oesterlin[2] in their studies of the action of anti-malarial drugs have suggested the potential value of this method for the diagnosis of malarial infections from blood smears. Subsequent work by the authors has demonstrated that the human parasite, *Plasmodium vivax*,[3] and the organisms of bird malaria, *P. nucleophilum*,[4] and *Haemoproteus* sp.[5] (from California Valley quail) can be stained in a satisfactory manner with fluorescent dyes.

Due to the large size of the parasite and the supply of the *Haemoproteus*, the bulk of the work in these laboratories has been done with this organism.

During the course of investigation positive staining reactions were observed with six fluorochromes. These were applied from saturated aqueous solutions to smears fixed in methyl alcohol as for Giemsa staining. The staining time is from two to five minutes. Alcoholic solutions can be substituted if the smears tend to wash off the slides with the aqueous stain. The six stains and their effectiveness in differentiating *Haemoproteus* are listed in Table 1.

TABLE 1

Stain	Nuclear color	Parasite color	Leucocyte color	Staining intensity
Beberine sulfate	Bright yellow	Golden	Yellow	+++
*Rivanol	Yellow green	Yellow green	Bright yellow	+++
Primulin	Blue	Blue white	Yellow	+++
Coriphosphine 0	Orange	Orange	Bright orange	++
Thioflavin	Yellow	Yellow	Yellow	++
Auramine 0	Yellow	Blue-white	Bright yellow	+

* 2-Ethoxy-6, 9-diamino acridine lactate.

Altering the pH of the staining medium with phosphate buffers showed a very slight increase in staining intensity in the alkaline region.

The apparatus necessary for fluorescence investigations of this nature is relatively simple. The principal innovation in equipment from ordinary microscopy is the use of a G.E. type H-4 high pressure mercury vapor lamp as the light source and a Corning filter No. 5840 which transmits the light between wavelengths of 310 mμ to 394 mμ. Ultraviolet light in this region is invisible but excites fluorescence in the fluorochromes.

The advantages of this technique if developed for the diagnosis of human malaria are many. The staining process is short, simple and reliable; the parasites, if present, stand out brilliantly as brightly fluorescent objects against a dark field; *Haemoproteus* of bird malaria and the *Plasmodia* of human malaria are readily discernible with dry lenses at magnifications not in excess of 200×; and the factor of eyestrain is greatly reduced.

Circumstances do not permit the full development of these techniques as applied to malarial diagnosis in this laboratory. All the results thus far obtained indicate that the method offers great possibilities in enhancing both the speed and accuracy of malarial diagnosis from blood smears. It also offers an interesting technique for the study of anti-malarial drugs (many of which are fluorescent) and their action upon the parasites.

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[17] A. S. Wiener, *Amer. Jour. Clin. Path.*, in press.

[1] P. K. H. Hagemann, *Munch. Med. Wschr.*, 85: 1066, 1938.

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[3] Furnished by Dr. Martin D. Young and Dr. Mark F. Boyd, U. S. Public Health Service and Rockefeller Foundation, respectively.

[4] Furnished by Dr. R. D. Manwell, Syracuse University.

[5] Furnished by Dr. C. M. Herman, Division of Fish and Game, State of California.

[6] Now with the Tennessee Valley Authority, Wilson Dam, Alabama.

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